REMARKS

Applicants respectfully request entry of the amendments and remarks submitted herein. No claims have been amended. The specification has been amended to incorporate matter deemed essential by the Examiner. Claims 1-17 are currently pending. Attached is a marked-up version of the changes being made by the current amendments. Reconsideration of the pending application is respectfully requested.

Sequence Compliance

Applicants have herein amended the specification to make reference to the amino acid sequence of concanavalin A used by Reeke et al. Therefore, the residues recited in claim 6 are with reference to the amino acid sequence as now cited in the specification. Accordingly, Applicants submit that claim 6 does not require a sequence identifier or a corresponding Sequence Listing.

Incorporation by Reference

The Examiner asserted that the incorporation of essential material into the specification by reference to a publication (*i.e.*, Reeke et al.), to exemplify the structure of recombinant reduced valency concanavalin A, is improper. Applicants have herein amended the specification to make reference to the concanavalin A amino acid sequence used by Reeke et al. The undersigned agent for Applicants declares that the amendatory material consists of the same material incorporated by reference in the referencing application.

The 35 U.S.C. §112 Rejections

Claims 1-17 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

The Examiner stated that the specification fails to provide adequate written description because the specification does not disclose representative species of fragments and analogs sufficient to establish that the Applicant had possession of the claimed fragments and analogs; because the specification does not contain a written description of each recombinant reduced valency CBL for use in a method of evaluating a carbohydrate; and because the specification fails to describe and define specific structures in amino acid sequences of multimeric molecules that can be altered or mutated.

With respect to the Examiner's assertion that Applicants were not in possession of the claimed fragments and analogs of recombinant reduced valency CBLs, Applicants submit that none of the pending claims recite either a fragment or an analog of recombinant reduced valency CBLs. The claims, however, recite a "recombinant reduced valency CBL", which is defined in the specification as "ligands which have been genetically engineered to have less than the normal valency" (please see page 23, lines 24-25). Applicants do not claim fragments and analogs of recombinant reduced valency CBLs.

With respect to the Examiner's assertion that the specification does not contain a written description of each recombinant reduced valency CBL, Applicants submit that the written description guidelines do not require that each and every species of a genus be disclosed. For a genus claim, the written description guidelines require that a "representative number of species" be sufficiently described. According to the written description guidelines, a "representative number of species" is that number which is "representative of the entire genus." Applicants refer the Examiner to Table I on pages 25-26, which provides written description for representative lectins from 11 different species. Such lectins can be recombinantly engineered by one of skill in the art (using methods disclosed in the specification) and the resulting recombinant reduced valency CBLs used in the methods of the invention. Applicants, therefore, have met the written description requirement for the claimed genus of recombinant reduced valency CBLs.

With respect to the Examiner's assertion that specific alterations in the amino acid sequence to be mutagenized are required for adequate written description, Applicants submit that the relevant sequences within CBLs for multimerization are known in the art or can be readily identified using methods known in the art. For example, the representative lectins disclosed in Table I are well known to those of ordinary skill in the art, and many peer-reviewed journal

articles have been published that characterize the subunits and that describe multimerization. According to the written description guidelines, the specification need only describe in detail that which is new or not conventional. Applicants submit that identifying positions involved in multimerization in CBLs, and designing and generating mutants to block multimerization, is conventional in the art and the specification therefore meets the written description requirement.

The Examiner further stated that adequate written description requires more than a mere statement of requisite use of recombinant reduced valency CBLs as part of the invention and a reference to a potential method of making it. The Examiner indicates that the nucleic acid sequence itself is required, and cites *Fiers v. Revel* and *Amgen v. Chugai Pharmaceutical.* Applicants strongly disagree with the Examiner's requirement for nucleic acid sequences in order that adequate written description be provided for the claimed invention. Applicants submit that the amino acid sequence of concanavalin A, as well as other CBLs, are known in the art. Applicants respectfully refer the Examiner to Tables II and II (pages 28 and 29), which disclose numerous residues in concanavalin A that can be modified to disrupt multimerization. Therefore, Applicants have disclosed the structure of a representative number of species that reflect the scope of the claimed genus of recombinant reduced valency CBLs.

In addition, the written description guidelines indicate that a description as filed is presumed to be adequate unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. In view of the remarks above, the Examiner has not met the burden of showing a lack of adequate written description for the pending claims, and Applicants therefore request that the rejection of claims 1-17 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 1-17 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is respectfully traversed.

The Examiner cited *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) for guidance in considering whether a disclosure would require undue experimentation. Factors in determining undue experimentation according to *In re Wands* include: (1) the nature of the invention, (2) the

state of the prior art, (3) the predictability or unpredictability of the art, (4) the amount of direction or guidance presented, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

With respect to the nature of the invention, Applicants do not disagree with the Examiner's general summary of the invention.

With respect to the state of the prior art, Applicants do not disagree with the Examiner's summary that the prior art fails to disclose the methods recited in claims 1 and 15.

With respect to the predictability or unpredictability of the art, the Examiner stated that there is no predicatability based on the instant specification that the claimed recombinant reduced valency CBLs have the active epitopic sites that can reversibly bind carbohydrates so as to allow quantitation of the amount of carbohydrate in a given sample. Applicants respectfully refer the Examiner to Tables II and III of the specification (pages 28 and 29), which disclose residues important in multimerization of concanavalin A. These residues were identified by x-ray crystallography of concanavalin A (Reeke et al.). Applicants submit that in conjunction with published crystallography data for various CBLs (see, for example, the references cited on page 27), the methods disclosed in the instant specification for mutagenesis of CBLs as well as screening recombinant reduced valency CBLs for reduced carbohydrate binding actually provides a high level of predictability in producing recombinant reduced valency CBLs that retain the ability to bind carbohydrates.

With respect to the amount of direction or guidance presented, the Examiner stated that the specification provides appropriate guidance for using a concanavalin A mutagenized at specific amino acid positions. The Examiner also stated that the specification lacks guidance for producing a recombinant reduced valency CBL by properly isolating the active epitopic sites that can bind carbohydrates. Applicants submit that the disclosure is not directed toward isolating the epitopes that can bind carbohydrates. Contrary to the Examiner's assertion, the disclosure is directed toward reducing the number of subunits to thereby reduce the number of carbohydrate-binding sites. Pages 23-37 provide an abundance of guidance for producing recombinant reduced valency CBLs for use in the methods of the invention.

With respect to the presence or absence of working examples, the Examiner stated that there are no working examples provided in the specification that show how to make the recombinant reduced valency CBLs. Applicants submit that working examples are not required. *In re Borkowski* 164 USPQ 642, 645 (CCPA 1970). The instant specification, however, defines a recombinant reduced valency CBL and discloses how to mutate a sequence to obtain a recombinant reduced valency CBL, how to express a mutated sequence to produce a recombinant reduced valency CBL, and how to screen recombinant reduced valency CBLs for reduced carbohydrate binding (see, for example, pages 23-40).

With respect to the quantity of experimentation necessary, the Examiner stated that it would require an undue amount of experimentation for the skilled artisan to make and use the methods as claimed. Applicants respectfully disagree, and submit that the specification discloses how to make recombinant reduced valency CBLs and how to evaluate such recombinant reduced valency CBLs, as well as how to perform each and every step of the claimed methods. See, for example, pages 23-40, and Figures 3 and 4.

With respect to the relative skill of those in the art, Applicants agree with the Examiner that the level of skill in this art is high.

With respect to the breadth of the claims, the Examiner stated that the overall structure of the molecules encompassing the broad genus of different CBLs is not taught. Applicants respectfully disagree, and refer the Examiner to page 23, line 26 through page 24, line 19, which describes the structural and functional characteristics of the claimed recombinant reduced valency CBLs. The Examiner further stated that the genus claim encompassing recombinant reduced valency CBL is enabled in and of itself, but is not enabled for species drawn to analogs and fragments of the CBL structure. As stated above, Applicant's claims are not directed toward analogs and fragments of recombinant reduced valency CBLs. Therefore, Applicants' claims are fully enabled based upon the disclosure (see, for example, pages 23-40).

The Examiner further stated that there is no experimental evidence provided that would indicate that the claimed method would work with any recombinant reduced valency CBL other than the recombinant reduced valency concanavalin A obtained from the concanavalin A structure taught by Reeke et al. Applicants respectfully disagree with the Examiner, and submit that not only do Applicants disclose methods that can be used to generate recombinant reduced

valency CBLs (see, for example, pages 23-37), but Applicants further disclose methods of screening recombinant reduced valency CBLs for reduced carbohydrate binding (see, for example, pages 37-40). Given that the relative level of skill in this art is high and that a screening method is disclosed for identifying suitable recombinant reduced valency CBLs, one of ordinary skill in the art could readily determine that a recombinant reduced valency CBL retained carbohydrate binding function.

The remarks submitted herein demonstrate that the claimed invention is fully enabled and would not require undue experimentation. Accordingly, Applicants respectfully request that the rejection of claims 1-17 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claim 6 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. This rejection is respectfully traversed.

The Examiner stated that claim 6 is indefinite because it does not specifically recite an amino acid sequence that defines the context of the claimed concanavalin A. The Examiner stated that claim 6 is further indefinite in failing to designate an amino acid sequence identifier for the structure encompassing the claimed concanavalin A. Applicants have herein amended the specification to make reference to the concanavalin A amino acid sequence used by Reeke et al. Applicants submit that the residues recited in claim 6 are with respect to the amino acid sequence now cited in the instant specification. Applicants submit, therefore, that claim 6 is not indefinite, and Applicants respectfully request that the rejection of claim 6 under 35 U.S.C. §112, second paragraph, be withdrawn.

CONCLUSION

Applicant asks that claims 1-17 be allowed. Enclosed is a $460 check for a Three-Month Petition for Extension of Time fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: September 19, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The specification on page 27, lines 21-29 has been amended as follows:

Several types of interactions are involved in producing and stabilizing dimeric Concanavalin A (see Table II below) or tetrameric Concanavalin A (see Table III below). For example, Reeke *et al.*, *supra*, describe residues from four distinct regions of the Concanavalin A structure that participate in forming contacts between monomeric subunits in dimeric Concanavalin A. Based upon this structure, the four regions include amino acid residues: 87-90, 136-139, and 175-178 (amino acid positions are by reference to the amino acid sequence data in Edelman et al., 1972, *Proc. Natl. Acad. Sci. U.S.A.*, 69:2580-4; Wang et al., 1975, *J. Biol. Chem.*, 250:1490-1502; and Cunningham et al., 1975, *J. Biol. Chem.*, 250:1503-12), which are located in the front of the monomeric Concanavalin A subunit. In contrast, amino acidresidues 117-132 are located at the back of the monomeric Concanavalin A subunit.